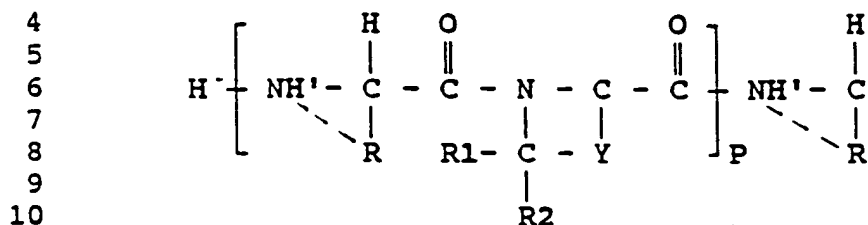


Prelim

1 An inhibitor compound, having the structure

2 Group I - Group II

3 where Group I has the structure:



11 wherein each R, independently, is chosen from the
12 group consisting of the R groups of an amino acid including
13 proline; each broken line, independently, represents a bond
14 to an H or a bond to one said R group, and each H'
15 represents said bond or a hydrogen; p is an integer between
16 0 and 4 inclusive;

17 or Group I has the structure:



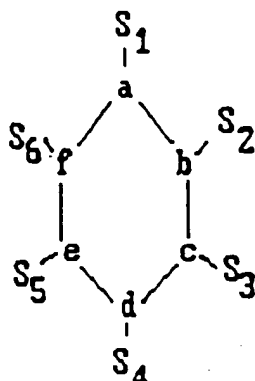
23 where n is between 0 and 3 inclusive,
24 each G2 and G3 independently is H or C1 - 3 alkyl,
25 G1 is NH3, NH - C - NH2, or



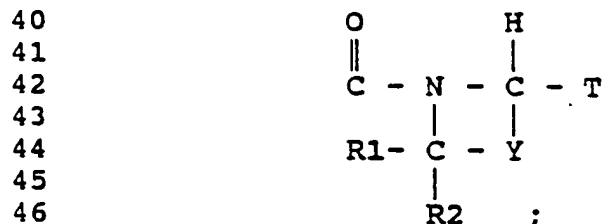
29 NG4, where G4 is C - G5
30
31

$$\begin{array}{c} | \\ \text{G6} \end{array}$$

32 where G5 and G6 can be NH, H, or C1 - 3 alkyl or
33 alkenyl with one or more carbons substituted with a
34 nitrogen; provided that G1 bears a charge and G1 and Group
35 II do not form a covalently bonded ring structure at pH 7.0;
36 or Group I has the structure:

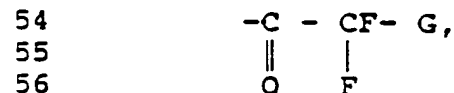


37 where one or two of said a, b, c, d, e, and f is N
 38 and the rest are C, and each S1 - S6 independently is H or
 39 C1 - C3 alkyl; where Group II has the structure:



47 T is a group of the formula:

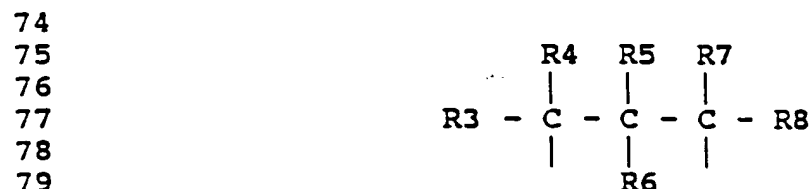
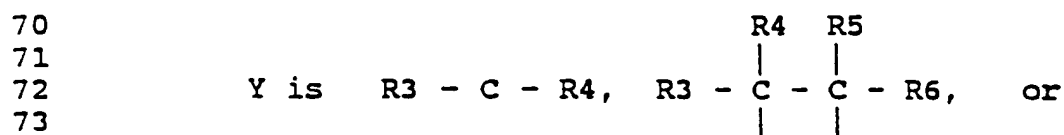
48 D2
 49 $|$
 50 - B- D1, where B is boron and each D1 and D2, independently,
 51 is a hydroxyl group or a group which is capable of being
 52 hydrolysed to a hydroxyl group in aqueous solution at
 53 physiological pH; a group of the formula:



57 where G is either H, F or an alkyl group containing 1 to 20
 58 carbon atoms and optional heteroatoms which can be N, S, or
 59 O; or a phosphonate group of the formula:



where each J, independently, is O-alkyl, N-alkyl, or alkyl, each said O-alkyl, N-alkyl or alkyl comprising 1 - 20 carbon atoms and, optionally, heteroatoms which can be N, S, or O; said T being able to form a complex with the catalytic site of a dipeptidyl-aminopeptidase type IV (DP IV) enzyme;



and each R₁, R₂, R₃, R₄, R₅, R₆, R₇, and R₈, separately is a group which does not significantly interfere with site specific recognition of said inhibitory compound by said DP IV, and allows said complex to be formed with said DP IV.

~~2.~~ ^{Prelim} The compound of claim 1, wherein T is a boronate group.

~~3.~~ The compound of claim 1, wherein T is a phosphonate group or a trifluoroalkyl ketone group.

~~4.~~ The compound of claim 1 wherein each R₁ - R₈ is H.

*Cancelled in
Dickinson*
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1 ~~5.~~ The compound of claim 1 or 2 wherein each R1 and
2 R2 are H, and each Y is CH₂ - CH₂.

1 ~~6.~~ The compound of claim 5 wherein each R is
2 independently chosen from the R group of proline and
3 alanine.

1 ~~7.~~ The compound of claim 1, wherein said compound
2 has a binding or dissociation constant to said DP IV of at
3 least 10⁻⁹M.

1 ~~8.~~ The compound of claim 1, wherein said compound
2 has a binding constant to said DP IV of at least 10⁻⁸M.

1 ~~9.~~ The compound of claim 1 admixed within a
2 pharmaceutically acceptable carrier substance.

1 ~~10.~~ The compound of claim 1 wherein, each D1 and D2
2 is, independently, F or D1 and D2 together are a ring
3 containing 1 to about 20 carbon atoms, and optionally
4 heteroatoms which can be N, S, or O.

1 ~~11.~~ A method for inhibiting DP IV in a mammal,
2 comprising administering to said mammal an effective amount
3 of a compound of claim 1.

1 ~~12.~~ The method of claim 11 wherein said amount is 1
2 - 500 mg/kg/day.

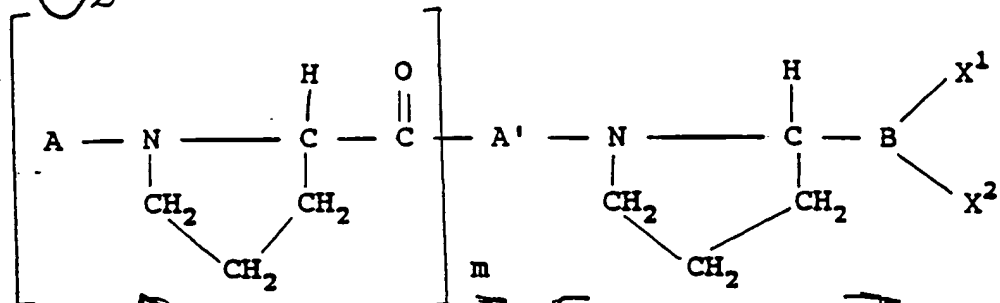
Claims as filed

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708

(Amended) - 28 -
13.

An inhibitor of DP-IV, having the structure:



hydroxyl group or a group capable of being hydrolysed to a hydroxyl group at physiological pH.

14. The inhibitor of claim 13 wherein A and A' are independently proline or alanine residues.

15. The inhibitor of claim 13 wherein m is 0.

16. The inhibitor of claim 13 wherein X¹ and X² are hydroxyl groups.

17. The inhibitor of claim 13 wherein said inhibitor is L-Ala-L-boroPro.

18. The inhibitor of claim 13 wherein said inhibitor is L-Pro-L-boroPro.

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Cancelled
via
election of
L-Pro-L-boroPro

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1 ~~19~~ X A method for inhibiting DP-IV in a mammal,
2 comprising administering to said mammal an effective amount
3 of a compound of claim 13.

1 ~~20~~ X. The method of claim 19 wherein said amount is
2 1 mg/kg of said mammal per day to 500 mg/kg of said mammal
3 per day.